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Non-scarring alopecia

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What makes non-scarring alopecia challenging?

- It is hard for patients and clinicians both
- Multifactorial etiologies often
- Limited effective treatments
- Technically non-scarring is “reversible” but often it is still difficult to treat, and the lack of predictability can be very difficult to manage.

However,

- Fairly limited possible diagnoses, often with overlap
- Limited effective treatment options, with overlap
- Acceptance that sometimes we never quite understand WHY something happens is key.

Challenges (and how to overcome them)

- Correct diagnosis
  - Examine closely
  - Consider biopsy, but biopsy in the right place – know your pathologist
    - I like to review my slides personally
- Monitoring for effectiveness of treatment
  - Take pictures
- Time management
  - Very difficult to manage sometimes
  - Use patient advocacy groups and support groups
  - Handouts are also helpful

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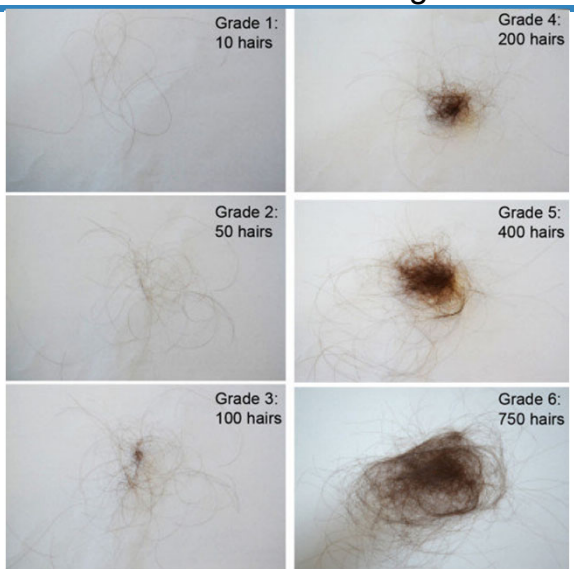
Objectives

- Define non-scarring alopecia
  - Define normal hair
- Discuss my approach to diagnosis of non-scarring alopecia
- Present cases
- Review management of non-scarring alopecia

What's normal about hair?

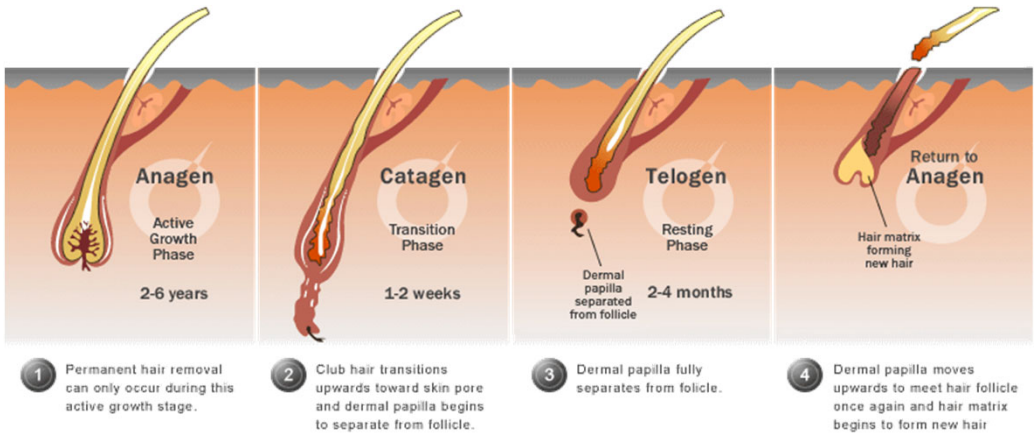
- Grows about 1 cm a month
- 10% in telogen (resting phase)
- 100-150,000 hairs per head
  - Blondes have more, red heads have less
  - Those of Asian and African descent also have thicker hair and less density
- About 100-200 hairs a day may be lost normally
  - **Substantial interindividual and seasonal variation**

Sinclair Hair Shedding Scale

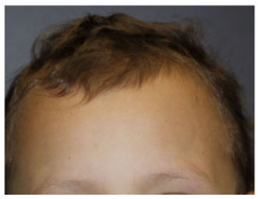


Kovacevic M, Goren A, Shapiro J, Sinclair R, Lonky NM, Situm M, Bulat V, Bolanca Z, McCoy J. Prevalence of hair shedding among women. Dermatol Ther. 2017 Jan;30(1):e12415. doi: 10.1111/dth.12415. Epub 2016 Oct 6. PMID: 27712018; PMCID: PMC6175177.

Normal hair cycle

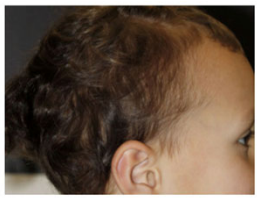


7-year-old girl with short anagen hair



Short anagen hair

Short anagen hair



Short anagen hair

Loose anagen syndrome

Non-scarring alopecia

- ***Androgenetic alopecia***
  - ***Female or male pattern hair loss***
- ***Alopecia areata***
- ***Telogen effluvium***
- Trichotillomania
- Post-operative (pressure-induced) alopecia
- Anagen effluvium
- Temporal triangular alopecia
- Senescent alopecia
- Permanent chemotherapy induced alopecia

Approach to the patient

Diagnosing alopecia

- History and physical
  - **Timing/duration, presence of increased shedding,** pattern of loss, associated symptoms
  - Scarring or non-scarring – dermoscopy helps
  - Hair pull test – 2 or more throughout scalp likely abnormal, regardless of last wash
- Laboratory evaluation
  - CBC, ferritin, TSH, Vitamin D (25,OH); sometimes testosterone
  - I typically do not order ANA unless other symptoms
- Histopathology
  - Two **4mm** punch biopsies, one for **horizontal** sectioning and one for vertical sectioning.

Biopsies

- When to biopsy?
  - Typically for non-scarring alopecia, it is patient preference, or treatment failure
- Where to biopsy?
  - Alopecia areata or trichotillomania – center of lesion is okay
  - Androgenetic alopecia or telogen effluvium – center of activity is okay – crown or vertex may be preferred.
- How to biopsy?
  - Two 4mm punch biopsies down through subcutaneous fat
  - Lidocaine with epinephrine and let it sit 15-30 minutes to reduce bleeding
  - Send one for horizontal sections and one for vertical sections
  - If you can only do one, send it for horizontal sections ONLY
  - An extra from a non-affected area for reference may be helpful

Table 4.1 Template for a "Scalp Biopsy Report"

Accession number:
Date:
Patient name/age/sex/race:
Submitting physician:
Clinical impression:
Macroscopic description: biopsy diameter/location on scalp: *e.g., 4 mm punch biopsy, vertex of scalp*
Microscopic description of vertical sections:
Microscopic description of horizontal sections:
Terminal anagen hairs:
Terminal catagen/telogen hairs:
Vellus hairs:
TOTAL hairs (terminal plus vellus, all phases):
Telogen count (terminal telogen hairs÷total terminal hairs):
Terminal: vellus ratio: *e.g., 3:1*
Inflammatory infiltrate (type and location): *e.g. upper follicle vs. lower follicle/bulb; lymphohistiocytic vs. neutrophilic; vacuolar interface type vs. no significant interface change; mild vs. dense*
Fibrosis or follicular scars (columns of connective tissue at the site of former follicles):
Additional features noted: *e.g., stelae, solar elastosis, follicular distortion, pigment incontinence, naked hair shafts*
Comments:
DIAGNOSIS:
Consultants:
Pathologist's signature _____

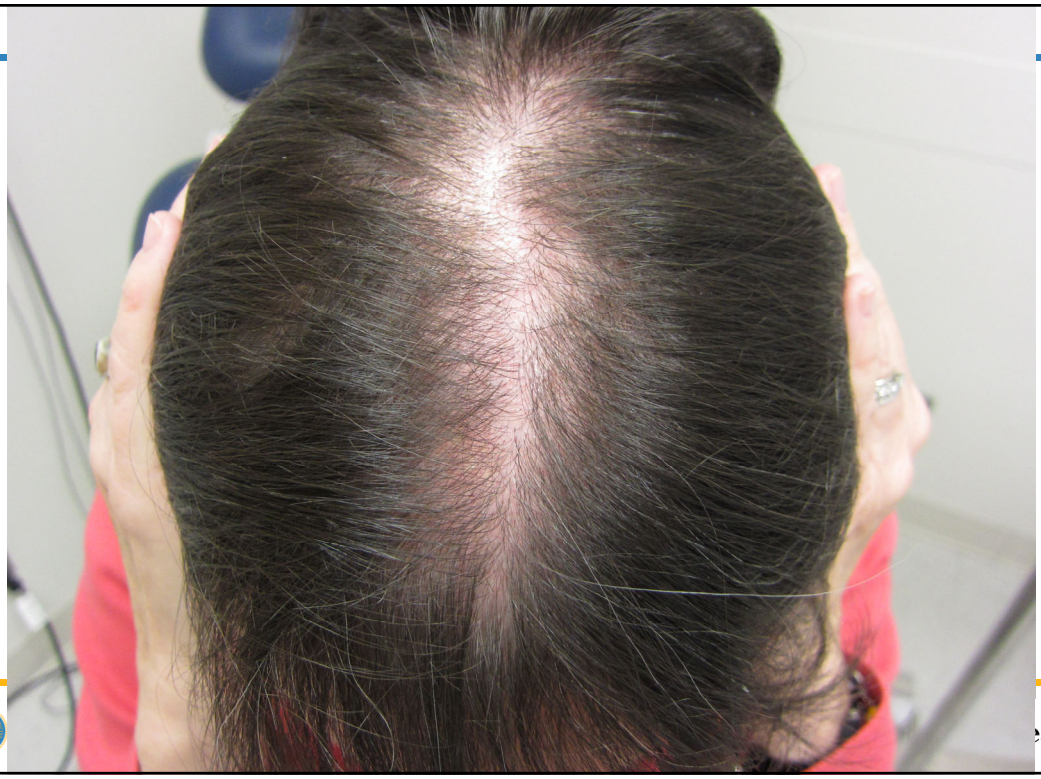
Sperling LC et al, An Atlas of Hair Pathology with Clinical Correlations. 2nd Ed. Informa healthcare, 2012.

Cases

Case 1

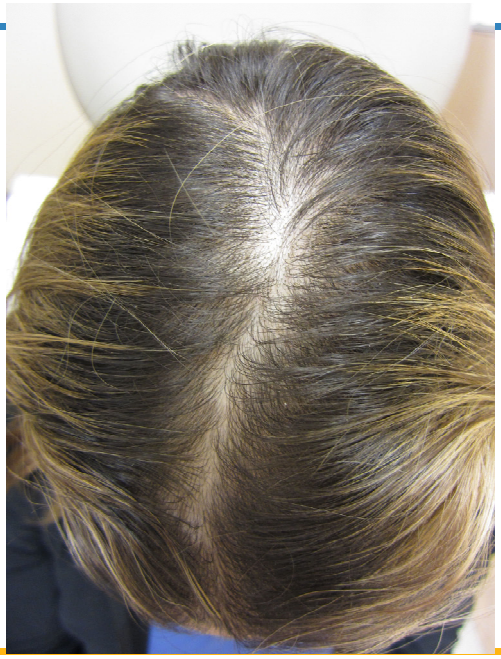
- 65 year old woman complains of 15 years of thinning hair especially over the crown of her scalp. There may be occasional pruritus, no pain or burning. There is no appreciable increase in shedding.

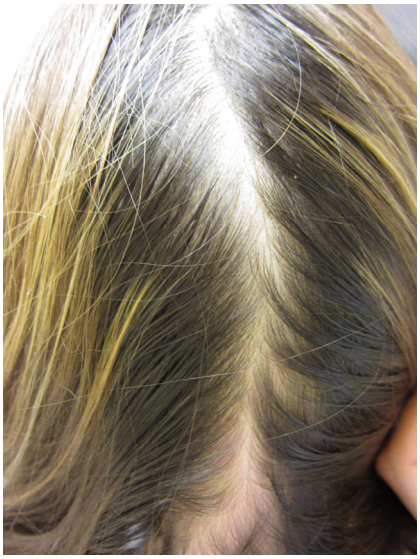
- (Cases 1-3 = diffuse hair loss, presented together for comparison)



Case 2

- 31-year-old woman presents with 2-3 weeks of excessive hair loss. “Clumps” of hair are noted by the patient. She has mild burning of her scalp.
- She got married 4 months ago, but has been trying to get pregnant for 10 months with fertility workup and IUI (intrauterine insemination), but no hormones. 6 months ago, she had surgery for a septate uterus. She also had COVID-19 infection 3 months ago.





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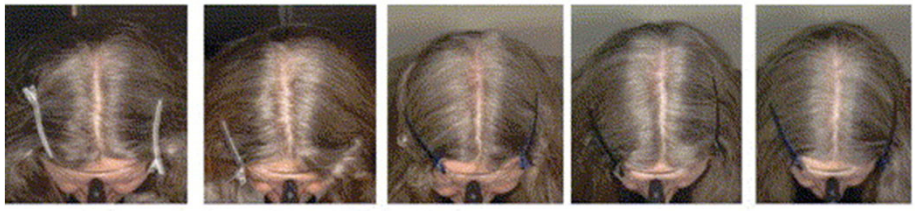
Case 3

- 54-year-old woman with 10 years of increased shedding of hair with “bald spots”. She is on no medications.
- She reports sensitivity of the scalp and redness.
- The shedding is constant.



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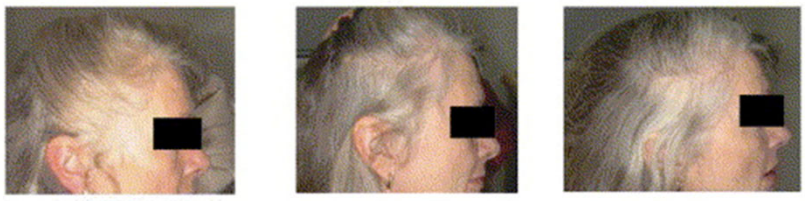

1999 2001 2003

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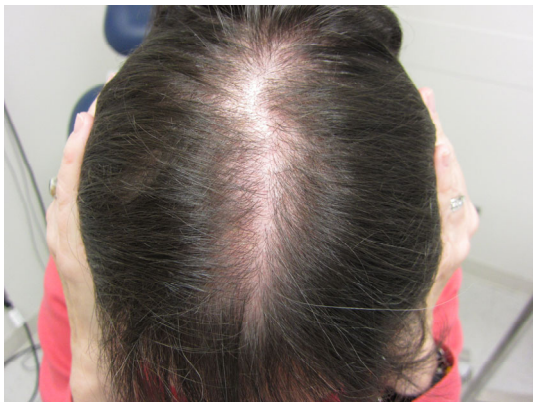
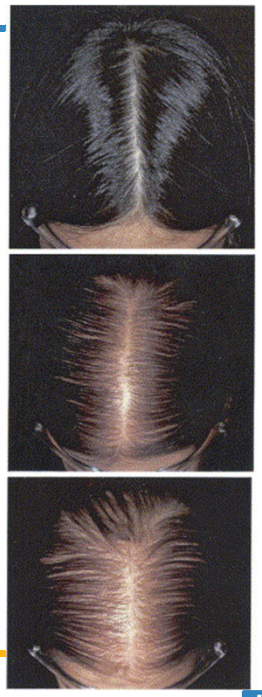
Most women with diffuse thinning:

- Androgenetic alopecia, female pattern hair loss, or senescent alopecia
- Telogen effluvium – acute vs. chronic
- Rarely – diffuse alopecia areata
- Might consider trichotillomania or even traction depending on the hairstyles chosen





1

2

3

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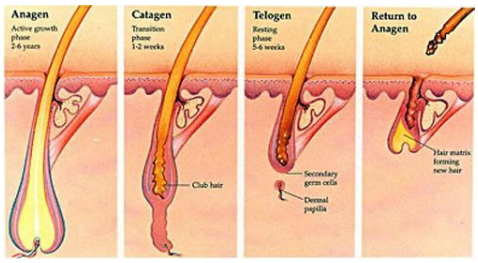
Androgenetic alopecia

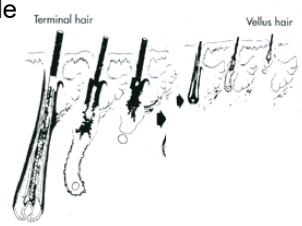
- Very common – may be considered normal variant, especially in men.
- In women, somewhat controversial, but one could consider three categories:
  - Puberty to age 40 = androgenetic alopecia, more likely androgen-mediated
  - ~Age 40-60 = female pattern hair loss, less clearly androgen-mediated, though often perimenopausal
  - Over age 60 = senescent alopecia, not likely androgen-mediated
  - May be important in determining treatment options
  - All show similar histopathology

Pathophysiology

Normal



Rapid miniaturization over one cycle



Progressive miniaturization over several cycles

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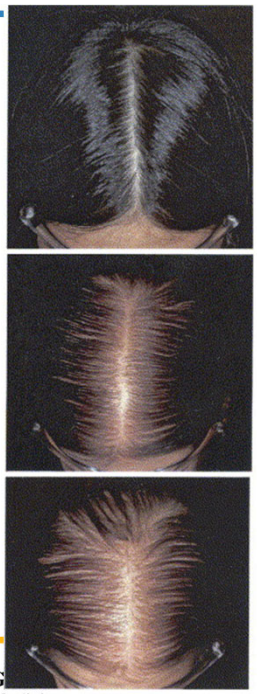

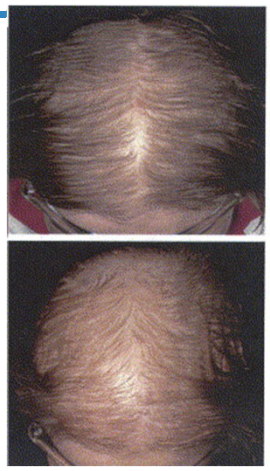

Fig 2. Five-point visual analogue scale for assessment of female hair loss. From Sinclair et al, The reliability of horizontally sectioned scalp biopsies in the diagnosis of chronic diffuse telogen hair loss in women.
J Am Acad Dermatol. 2004 Aug;51(2):189-99.

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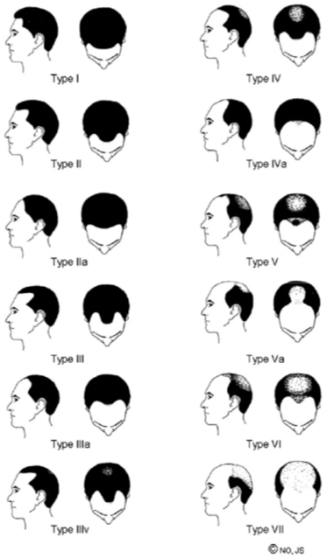
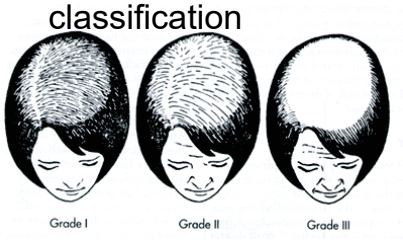
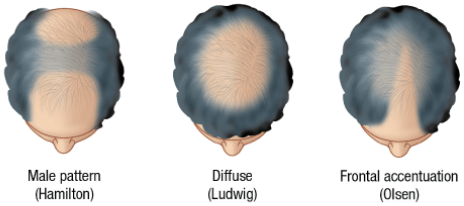
Norwood-Hamilton classification



Ludwig classification



Olsen EA, Female pattern hair loss, *J Am Acad Dermatol* 2001; 45:S70-80.



Source: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ: *Fitzpatrick's Dermatology in General Medicine*, 7th Edition: http://www.accessmedicine.com

Otberg N, Finner AM, Shapiro J, Androgenetic alopecia 2007;36:379-98.

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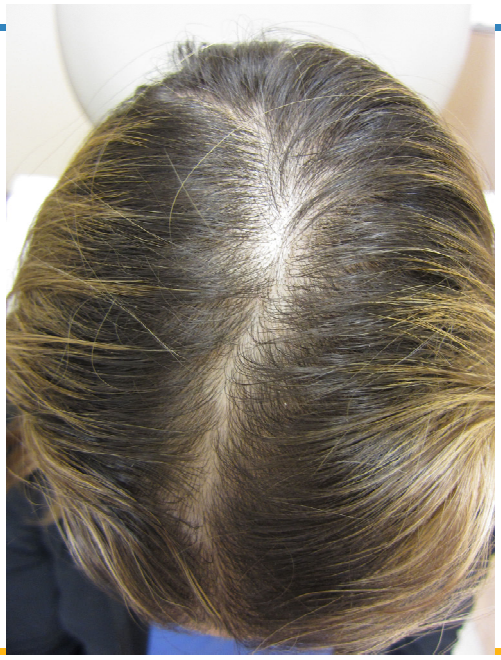

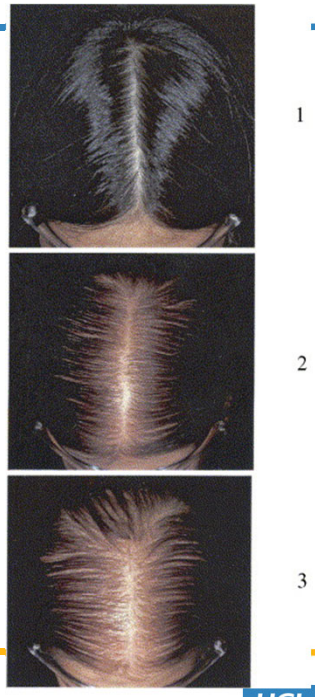

Telogen effluvium

- premature conversion of anagen hairs to telogen; or following prolonged anagen
- surgery, parturition, fever, drugs, dieting, or traction; primary scalp problem (i.e., psoriasis)
- Shedding occurs 3-5 months after the event, though sometimes as soon as a few weeks
- Shedding should last 3-6 months and then visible regrowth/recovery may take 3-6 months or more
- Rx: treat underlying problem, topical minoxidil, laser comb, or **simply monitor**

DRUG-INDUCED ALOPECIA	
Telogen phase	– **Anticoagulants**: heparin > warfarin – Anticonvulsants: carbamazepine, valproic acid, phenytoin – Antidepressants: imipramine, desipramine, maprotiline, fluoxetine – Antihypertensive agents: **β-blockers**: acebutolol, propranolol ACE inhibitors: captopril, enalapril Diuretics: spironolactone – Antimicrobials: gentamicin, thiamphenicol, fluconazole – Antithyroid drugs: carbimazole, thiouracils – Colchicine – Interferons – Lipid-lowering agents: clofibrate, cholestyramine – **Lithium** – NSAIDs: piroxicam, naproxen, indomethacin, ibuprofen – Oral contraceptives – **Retinoids** – Others: allopurinol, cimetidine, L-dopa, amphetamines, pyridostigmine, bromocriptine
Anagen phase	– Antineoplastic agents (see Table 22.8) – Others: arsenic, bismuth, gold, thallium

Table 22.7 Drug-induced alopecia. ACE, angiotensin-converting enzyme.

From Bolognia, Jorizzo & Rapini: Dermatology 2e. © 2008 Elsevier, Ltd.

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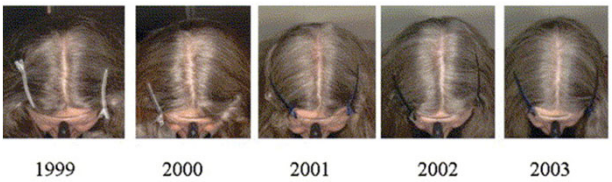

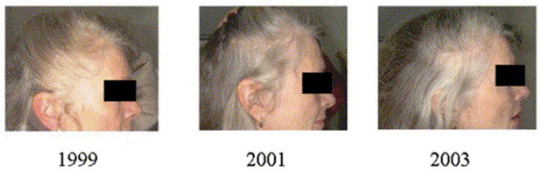

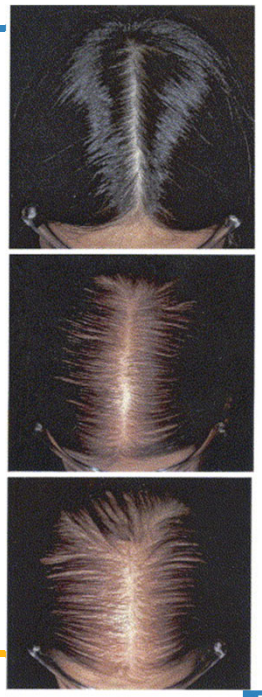

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Chronic telogen effluvium

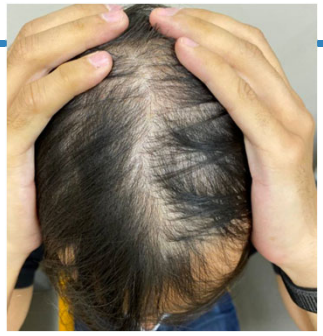
- diffuse generalized shedding with thinning of scalp hair; lasts longer than 6 months
- 30–60 years of age, mostly women
- hair loss starts abruptly
- fluctuating course and diffuse thinning of the hair all over the scalp with bitemporal and vertex prominence
- no discernible cause
- Terminal: vellus hair ratio = 8:1 or more
- may respond to topical minoxidil
- May be a precursor to androgenetic alopecia/FPHL/senescent alopecia

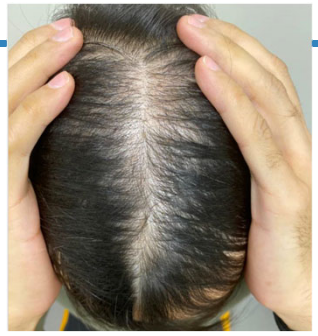
Treatment for diffuse thinning

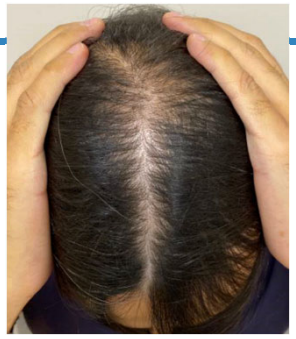
- Treat scalp problems (i.e., seborrheic dermatitis)
  - Zinc pyrithione shampoo or other antiseborrheic shampoos
  - Ketoconazole shampoo (1% OTC, 2% Rx)
- Hair growth promoters
  - Topical (2% solution or 5% solution (men's) or foam (men's or women's)) or low dose oral minoxidil (0.25 mg to 2.5 mg daily)
  - Topical bimatoprost or latanoprost
  - Laser comb, band, or cap
- If applicable, antiandrogen therapy
  - Spironolactone
  - Finasteride, dutasteride
  - Flutamide, bicalutamide
- Microneedling, platelet rich plasma therapy
- Hair restoration surgery – select cases

7/2020 7/2021

32 year old female
Spironolactone 150 mg daily
Minoxidil 0.625 mg daily
Ketoconazole shampoo 2% three times a week
On drospirenone-ethinyl estradiol OCP





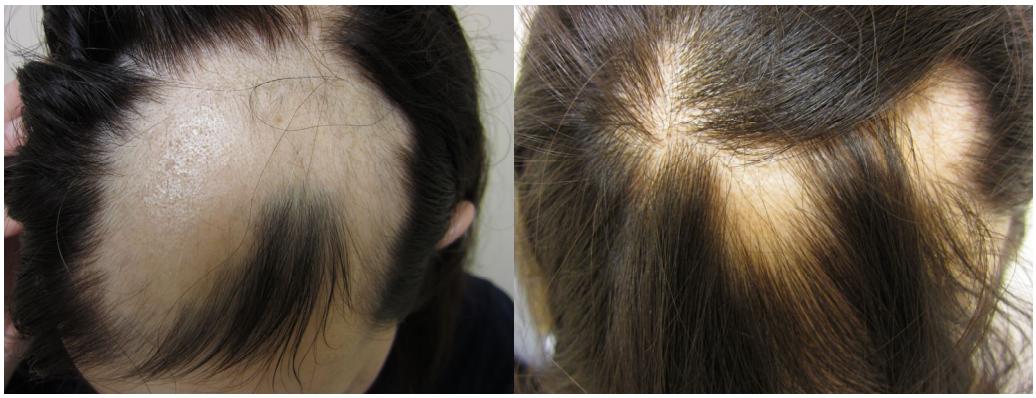


9/2020 1/2021 7/2021

36 year old male
Dutasteride 0.5 mg daily
Ketoconazole 2% shampoo every other day
Platelet rich plasma therapy

Case 4

- 45-year-old woman with 6 months of hair loss “in patches” with no pain.
- She was on vacation when it started.
- No medications, no other medical problems.
- No body hair loss noted.



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Alopecia areata

- Non-scarring patchy alopecia
- Autoimmune cell-mediated process thought to be due to loss of immune privilege in the anagen hair bulb
- Genetic polymorphisms have been identified
- Path: “swarm of bees” or a few bees (lymphocytes) around the hair bulb; the key is markedly increased telogen/catagen

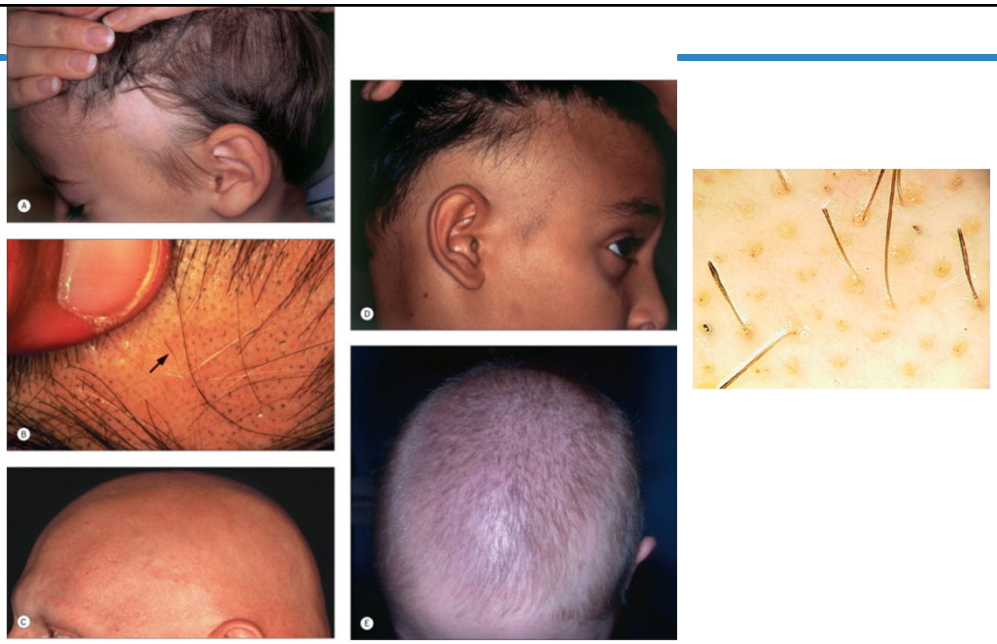

Fig. 68.7 Alopecia areata. A Circular area of alopecia in a child. **B** Exclamation point hair with the distal end broader than the proximal end. **C** Total alopecia of scalp, eyebrows and eyelashes in a patient with alopecia universalis. **D** Ophiasis with a band-like pattern of hair loss along the periphery of the temporal and occipital scalp. **E** Diffuse variant of alopecia areata. *E, Courtesy of Maria K Hordinsky MD.*

Tosti A, Gray J. *Journal of Investigative Dermatology Symposium Proceedings* (2007) **12,** 23–27.

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Table II. Alopecia Areata Scale

Scalp hair loss	
Severity	**Extent of scalp hair loss**
Mild AA	20% or less scalp hair loss
Moderate AA	21%-49% scalp hair loss
Severe AA	50%-100% scalp hair loss

If mild or moderate, increase AA severity rating by 1 level if 1 or more of the following is present:

- Negative impact on psychosocial functioning resulting from AA
- Noticeable involvement of eyebrows or eyelashes
- Inadequate response after at least 6 months of treatment
- Diffuse (multifocal) positive hair pull test consistent with rapidly progressive AA

AA, Alopecia areata.

King BA, Mesinkovska NA, Craiglow B, et al. Development of the alopecia areata scale for clinical use: Results of an academic-industry collaborative effort [published online ahead of print, 2021 Aug 30]. *J Am Acad Dermatol*. 2021;S0190-9622(21)02387-2. doi:10.1016/j.jaad.2021.08.043

41

Therapeutic ladder for alopecia areata

- Topical or intralesional corticosteroids
- Topical immunotherapy (DPCP, squaric acid)
- Topical minoxidil
- Topical anthralin cream
- Systemic corticosteroids
- Excimer laser
- Systemic immunosuppressants
  - JAK inhibitors, cyclosporine, methotrexate
- Other options, less evidence
  - Fexofenadine, platelet rich plasma therapy, simvastatin-ezetimibe

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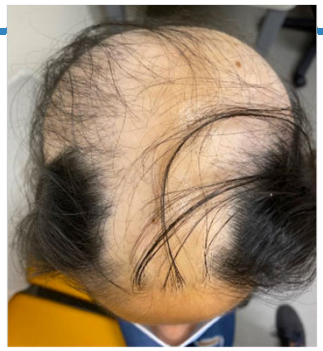
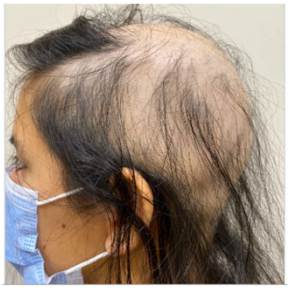
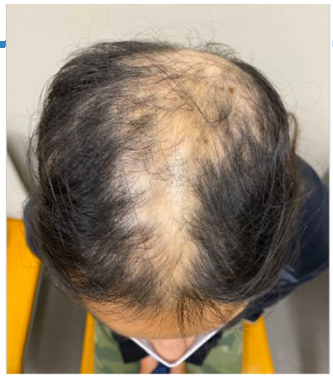


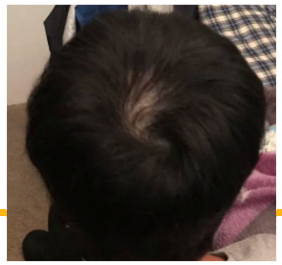




9/2020

12/2020

Topical corticosteroids and minoxidil foam



3/2021

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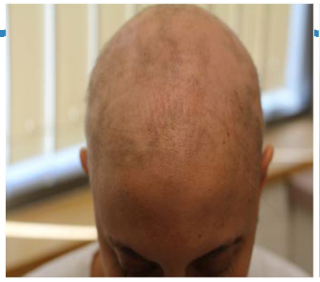
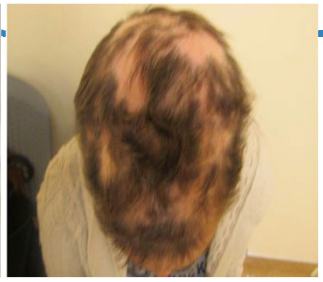
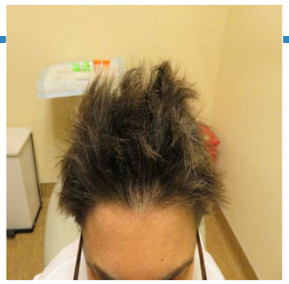


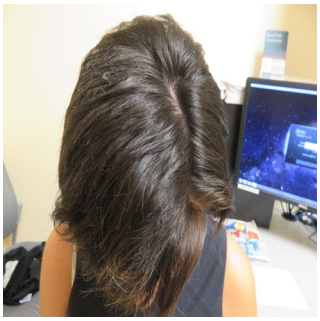




Baseline

1 month

4 months



9 months
Max dose oral tofacitinib 5 mg twice daily
Patchy alopecia recurred within 2 weeks of reducing dose

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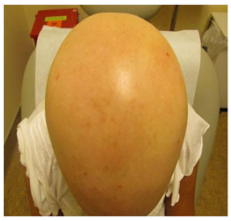
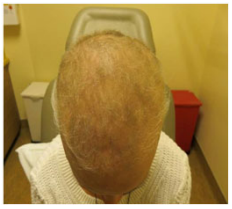
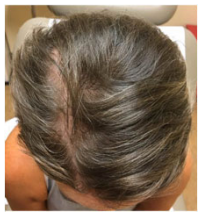
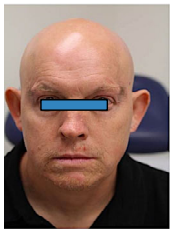
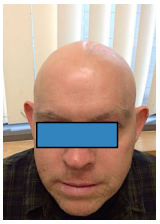
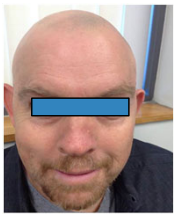
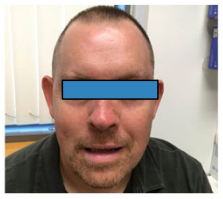
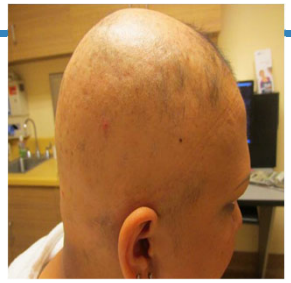
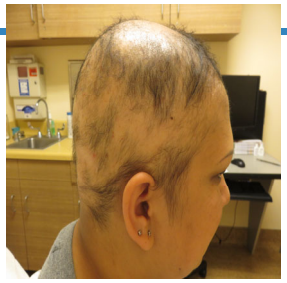
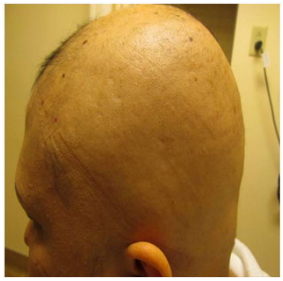
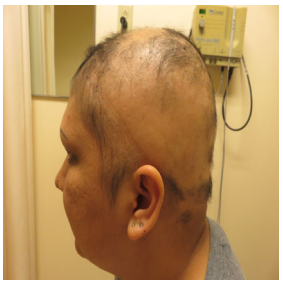




Baseline 3 months 9 months

Baseline 4 months 6 months 9 months

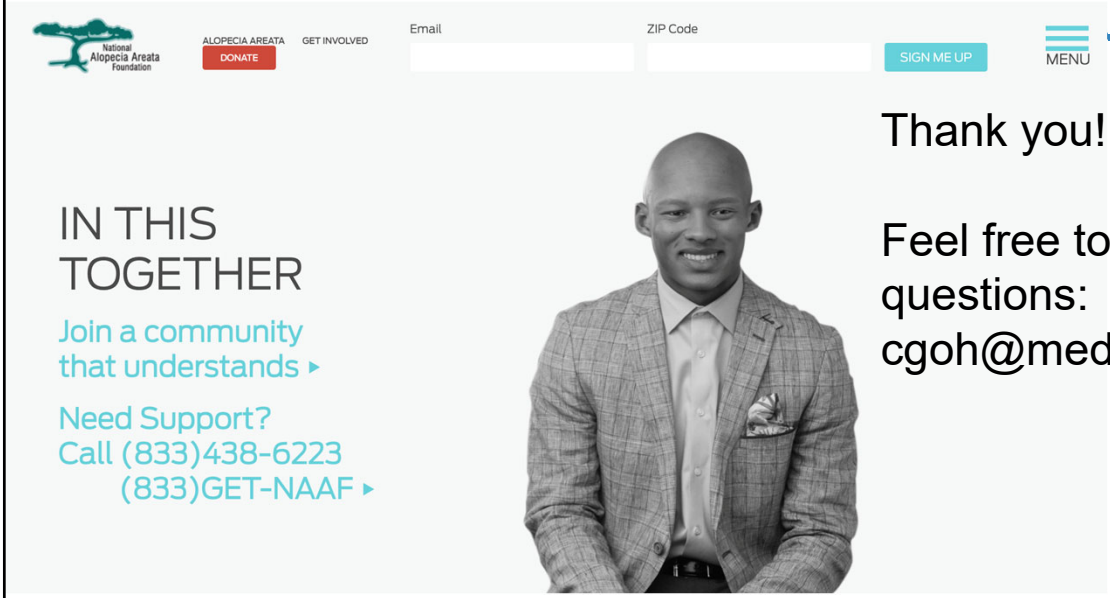
- No baseline photos
- Came at 6 months of treatment – up to 10 mg twice daily of tofacitinib.
- Started monthly intralesional triamcinolone injections focally, more on right scalp
- Within the next year, 100% regrowth, back to tofacitinib 5 mg twice daily.

9 months 10 months

Non-scarring alopecia pearls/summary

- Diffuse hair thinning is common and often has a lot of overlap
- Topical minoxidil is still the only FDA approved treatment for female pattern hair loss
- Low dose oral minoxidil can be used, but may be comparable in efficacy
- Traditional and conservative treatments can be effective
- Janus kinase inhibitors appear to be effective in the treatment of alopecia areata
- Clinical trials for JAK inhibitors and other molecules are underway



Thank you!

Feel free to email with questions:
cgoh@mednet.ucla.edu

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